

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Klinman et al.

Application No. 10/666,022

Filed: September 17, 2003

Confirmation No. 7954

For: METHOD OF TREATING AND
PREVENTING INFECTIONS IN
IMMUNOCOMPROMISED SUBJECTS
WITH IMMUNOSTIMULATORY CPG
OLIGONUCLEOTIDES

Examiner: Nita Minnifield

Art Unit: 1645

Attorney Reference No. 4239-66899-01

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Agent
for Applicant(s)

Date Mailed December 10, 2004

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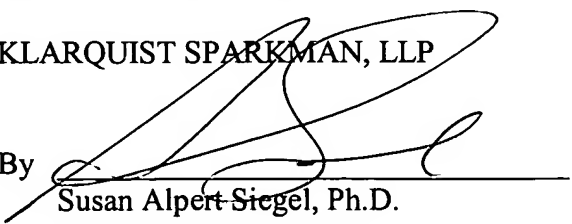
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- ☒ Second Supplemental Information Disclosure Statement
- ☒ Form 1449 and copies of references cited thereon (271)
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Respectfully submitted,

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**SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT
PURSUANT TO 37 C.F.R. § 1.97(b)(3)**

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Listed on the accompanying form PTO-1449 and enclosed herewith are several English-language documents. Applicants respectfully request that these documents be listed as references cited on the issued patent.

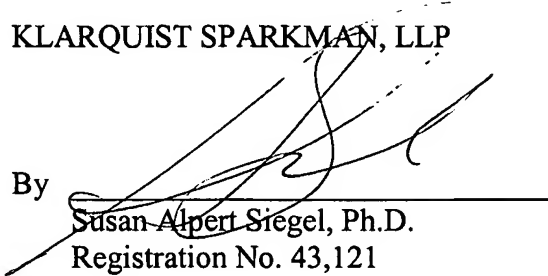
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The filing of this IDS shall not be construed to be an admission that the information cited in the statement is, or is considered to be, prior art or otherwise material to patentability as defined in 37 C.F.R. §1.56.

Respectfully submitted,

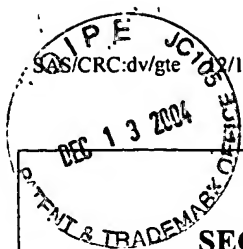
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First Named Inventor	Klinman
Art Unit	1645
Examiner Name	Nita Minnifield

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		ADYA, et al., "Expansion of CREB's DNA recognition specificity by Tax results from interaction with Ala-Ala-Arg at positions 282-284 near the conserved DNA-binding domain of CREB". Proc. Natl. Acad. Sci. USA 91(12):5642-5646 (1994).
		AGRAWAL, et al., "Pharmacokinetics of Oligonucleotides". Ciba. Found. Symp. 209:60-78 (1997), abstract only.
		AGRAWAL, et al., "Pharmacokinetics and Bioavailability of Antisense Oligonucleotides Following Oral and Colorectal Administration of Experimental Animals". Handb. Exp. Pharmacol.: Antisense Research and Application 131:525-543 (1998).
		AGRAWAL, "Antisense Oligonucleotides: Toward Clinical Trials". Tibtech 14:376-387 (1996).
		AGRAWAL, et al., "In Vivo Pharmacokinetics of Phosphorothioate Oligonucleotides Containing Contiguous Guanosines". Antisense & Nucleic Acid Drug Development 7:245-249 (1997).
		AGRAWAL, et al., "Absorption, Tissue Distribution and In Vivo Stability in Rats of a Hybrid Antisense Oligonucleotide Following Oral Administration". Biochemical Pharmacology 50(4):571-576 (1995).
		AGRAWAL, et al., "Pharmacokinetics of Antisense Oligonucleotides". Clin. Pharmacokinet 28(1):7 (1995).
		AGRAWAL, et al., "Antisense therapeutics: is it as simple as complementary base recognition?". Molecular Med. Today 6(2):72-81 (2000), abstract only.
		AGRAWAL, et al., "Pharmacokinetics, biodistribution, and stability of oligodeoxynucleotide phosphorothioates in mice". Proc. Natl. Acad. Sci. USA 88:7595-7599 (1991).
		AGRAWAL, "Medicinal Chemistry and Therapeutic Potential of CpG DNA". Trends in Molecular Medicine 8(3):114-121 (2002).
		ALAMA, et al., "Antisense Oligonucleotides as Therapeutic Agents". Pharmacol. Res. 36:171-178 (1997).
		ANDERSON, "Human Gene Therapy". Nature 392:25-30 (Apr. 1998).
		ANDERSON, et al., "TH2 and 'TH2-like' cells in allergy and asthma; pharmacological perspectives". TIPS 15:324-332 (1994).
		ANFOSSI, et al., "An oligomer complementary to c-myc-encoded mRNA inhibits proliferation of human myeloid leukemia cell lines". Proc. Natl. Acad. Sci. USA 86:3379-3383 (May 1989).
		ANGIER, "Microbe DNA seen as alien by immune system". New York Times Page C1, 2 pages (1995).
		AZAD, et al., "Antiviral activity of a phosphorothioate oligonucleotide complementary to RNA of the human cytomegalovirus major immediate-early region". Antimicrobial Agents and Chemotherapy 37:1945-1954 (1993).
		AZUMA, "Biochemical and immunological studies on cellular components of tubercle bacilli". Kekkaku 69(9):45-55 (1992).
		BALLAS, et al., "Induction of NK activity in murine and human cells by CpG motifs in oligodeoxynucleotides and bacterial DNA". J. Immunol. 157(5):1840-1845 (1996).

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		BANCHEREAU, et al., "Immunobiology of Dendritic Cells". Ann. Rev. Immunol. 18:767-811 (2000).	
		BANCHEREAU & STEINMAN, "Dendritic Cells and the Control of Immunity". Nature 392:245-252 (1998).	
		BAROUCH, et al., "Control of Viremia and Prevention of Clinical AIDS in Rhesus Monkeys by Cytokine-Augmented DNA Vaccination". Science 290:486-492 (Oct. 2000).	
		BAUER, et al., "Bacterial CpG-DNA Triggers Activation and Maturation of Human CD11c-, CD123+ Dendritic Cells". J. Immunol. 166:5000-5007 (2001).	
		BAYEVER, "Systemic administration of a phosphorothioate oligonucleotide with a sequence complementary to p53 for acute myelogenous leukemia and myelodysplastic syndrome: initial results of a Phase I trial". Antisense Res. Dev. 3:383-390 (1993).	
		BENIMETSKAYA, et al., "Formation of a G-tetrad and higher order structures correlates with biological activity of the RelA (NF-kBp65) 'antisense' oligodeoxynucleotide". Nucleic Acids Research 25(13):2648-2656 (1997).	
		BENNETT, et al., "DNA binding to human leukocytes: evidence for a receptor-mediated association, internalization, and degradation of DNA". J. Clin. Invest. 76(6):2182-2190 (1985).	
		BERG, et al., "Interleukin-10 is a central regulator for the response to LPS in murine models of endotoxic shock and the Shwartzman reaction but not endotoxin tolerance". J. Clin. Invest. 96(5):2339-2347 (1995).	
		BIOLABS, "1988-1989 Catalog, Random Primer #s 1230, 1601, 1602". ().	
		BISHOP, et al., "Intramolecular G-quartet Motifs Confer Nuclease Resistance to a Potent Anti-HIV Oligonucleotide". The Journal of Biological Chemistry 271(10):5698-5703 (Mar.1996).	
		BLANCHARD, et al., "Interferon- γ Induction by Lipopolysaccharide: Dependence of Interleukin 2 and Macrophages". The Journal of Immunology 136(3):963-970 (Feb. 1986).	
		BLANCO, et al., "Induction of Dendritic Cell Differentiation by IFN- α in Systemic Lupus Erythematosus". Science 294:1540-1543 (2001).	
		BLAXTER, et al., "Genes expressed in Brugia malayi infective third stage larvae". Mol. Biochem. Parasitol. 77:77-93 (1996).	
		BOGGS, et al., "Characterization and modulation of immune stimulation by modified oligonucleotides". Antisense Nucl. Acid Drug Dev. 7(5):461-471 (1997).	
		BOIARKINA, et al., "Dietary supplementals from ground fish meat with DNA for treatment and prophylaxis". Vopr. Pitan 1:29-31 (1998), abstract only.	
		BRANDA, et al., "Immune stimulation by an antisense oligomer complementary to the rev gene of HIV-1". Biochem. Pharmacol. 45(10):2037-2043 (1993).	
		BRANDA, et al., "Amplification of antibody production by phosphorothioate oligodeoxynucleotides". J. Lab Clin. Med. 128(3):329-338 (1996).	
		BRISKIN, et al., "Lipopolysaccharide-unresponsive mutant pre-B-cell lines blocked in NF-kappa B activation". Mol. Cell Bio. 10(1):422-425 (1990).	

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		BURGESS, "The antiproliferative activity of c-myb and c-myc antisense oligonucleotides in smooth muscle cells is caused by a nonantisense mechanism". Proc. Natl. Acad. Sci. USA 92:4051-4055 (Apr. 1995).	
		CALAROTA, et al., "Immune Responses in Asymptomatic HIV-1 Infected Patients After HIV-DNA Immunization Followed by Highly Active Antiretroviral Threatment". J. Immunol. 163(4):2330-2338 (1999).	
		CHACE, et al., "Regulation of differentiation in CD5+ and conventional B cells". Clin. Immunol. Immunopathol. 68(3):327-332 (1993).	
		CHANG, et al., "The palindromic series I repeats in the simian cytomegalovirus major immediate-early promoter behave as both strong basal enhancers and cyclic AMP response elements". J. Virol. 64(1):264-277 (1990).	
		CHAPUIS, et al., "Differentiation of Human Dendritic Cells from Monocytes in vitro". Eur. J. Immunol. 27:431-441 (1997).	
		CHU, et al., "CpG oligodeoxynucleotides act as adjuvants that switch on T helper 1 (Th1) immunity". J. Exp. Med. 186(10):1623-1631 (1997).	
		CHUN, et al., "Effect of interleukin-2 on the pool of latently infected, resting CD4+ T-cells in HIV-1-infected patients receiving highly active anti-retroviral therapy". Nature Med. 5(6):651-655 (1999).	
		CHUN, et al., "Perspective: Latent reservoirs of HIV: Obstacles to the eradication of virus". Proc. Natl. Acad. Sci. USA 96:10958-10961 (1999).	
		COHEN, et al., "Exploring How to Get at -- and Eradicate -- Hidden HIV". Science 279:1854-1855 (1998).	
		COHEN & FAUCI, et al., "HIV/AIDS in 1998 -- Gaining the Upper Hand?". JAMA 280(1):87-88 (1998).	
		COOK, et al., "Effect of a Single Ethanol Exposure on HIV Replication in Human Lymphocytes". J. Invest. Med. 45(5):265-271 (1997).	
		COOPER, et al., "Therapeutic Strategies for HIV Infection -- Time To Think Hard". The New England Journal of Medicine 339(18):1319-1321 (1998).	
		COWDERY, et al., "Bacterial DNA induces NKcells to produce IFN-gamma in vivo and increases the toxicity of lipopolysaccharides". J. Immunol. 156(12):4570-4575 (1996).	
		CROSBY, et al., "The early responses gene NGFI-C encodes a zinc finger transcriptional activator and is a member of the GCGGGGGCG (GSG) element-binding protein family". Mol. Cell Bio. 2:3835-3841 (1991).	
		CRYSTAL, "Transfer of genes to humans: early lessons and obstacles to success". Science 270:404-410 (1995).	
		CRYZ, et al., "Vaccine Delivery System -- European Commission COST/STD Initiative Report of the Expert Panel VII". Vaccine 14(7):665-690 (1996).	
		D'ANDREA, et al., "Interleukin 10 (IL-10) inhibits human lymphocyte interferon gamma-production by suppressing natural killer cell stimulatory factor/IL-12 synthesis in accessory cells". J. Exp. Med. 178(3):1041-1048 (1993).	
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		DAVEY, et al., "HIV-1 and T-Cell dynamics after interruption of highly antiretroviral therapy (HAART) in patients with a history of sustained viral suppression". Proc. Natl. Acad. Sci. USA 96(26):15109-15114 (1999).	
		DAVIS, et al., "CpG DNA is a Potent Enhancer of Specific Immunity in Mice Immunized with Recombinant Hepatitis B Surface Antigen". J. Immunol. 160(2):870-876 (1998).	
		DAVIS, "Plasmid DNA expression systems for the purpose of immunization". Curr. Opin. Biotechnol. 8(5):635-646 (Oct. 1997).	
		DEMATOS, et al., "Pulsing of Dendritic Cells with Cell Lysates from Either B16 Melanoma or MCA-106 Fibrosarcoma Yields Equally Effective Vaccines Against B16 Tumors in Mice". J. Surg. Oncol. 68:79-91 (1998).	
		DEML, et al., "Immunostimulatory CpG motifs trigger a T Helper-1 immune response to Human Immunodeficiency Virus Type-1 (HIV-1) gp160 envelope protein". Clin. Chem. Lab. Med. 37(3):199-204 (1999).	
		DIAS et al., "Antisense Oligonucleotides: Basic Concepts and Mechanisms," <i>Mol. Cancer Ther.</i> 1:317-355, 2002	
		DOERFLER, et al., "On the Insertion of Foreign DNA into Mammalian Genomes: Mechanism and Consequences". <i>Gene</i> 157(1-2):241-254 (1995), abstract only.	
		DURHAM, et al., "Immunotherapy and Allergic Inflammation". Clin. Exp. Allergy 21 Suppl 1:206-210 (1991).	
		ECK, et al., "Chapter 5: Gene-Based Therapy". Goodman & Gilman's The Pharmacological Basis of Therapeutics 9th ed.:77-101 (1996).	
		ELKINS, et al., "Bacterial DNA containing CpG motifs stimulates lymphocyte-dependent protection of mice against lethal infection with intracellular bacteria". J. Immunol. 162:2291-2298 (1999).	
		ENGLISCH, et al., "Chemically modified oligonucleotides as probes and inhibitors". Angew. Chem. Int. Ed. Engl. 30:613-629 (1991).	
		ERB, et al., "Infection of mice with Mycobacterium bovis-badillus Calmette-Guerin (BCG) supresses allergen-induced airway eosinophilia". J. Exp. Med. 184(4):561-569 (1998).	
		ETLINGER, "Carrier sequence selection--one key to successful vaccines". Immunology Today 13(2):52-55 (1992).	
		FANSLOW, et al., "Effect of Nucleotide Restriction and Supplementation on Resistance to Experimental Murine Candidiasis". J. Parenter. Enteral. Nutr. 12(1):49-52 Abstract (1988).	
		FIELDS, et al., "Murine Dendritic Cells Pulsed With Whole Tumor Lysates Mediate Potent Antitumor Immune Responses in vitro and in vivo". Proc. Natl. Acad. Sci. USA 95:9482-9487 (1998).	
		FILION, et al., "Major Limitations in the use of Cationic Liposomes for DNA Delivery". Int. J. Pharmaceuticals 162:159-170 (1998).	
		FOX, "Mechanism of action of hydroxychloroquine as an antirheumatic drug". Chem. Abstracts 120:15, Abstract No. 182630 (1 page) (1994).	

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		FREIDAG, et al., "CpG oligodeoxynucleotides and interleukin-12 improve the efficacy of Mycobacterium bovis BCG vaccination in mice challenged with M. tuberculosis". Infect. Immun. 68:2948-2953 (2000).	
		GAO, et al., "Phosphorothioate oligonucleotides are inhibitors of human DNA polymerases and Rnase H: Implications for antisense technology". Mol. Pharmacol. 41:223-229 (1992).	
		GARRAUD, "Regulation of Immunoglobulin Production in Hyper-IgE (Job's) Syndrome". J. Allergy Clin. Immunol. 103(2 Pt 1):333-340 (Feb. 1999).	
		GLUCKMAN, et al., "In Vitro Generation of Human Dendritic Cells and Cell Therapy". Cytokines Cell Mol. Ther. 3:187-196 (1997).	
		GRAMZINSKI, et al., "Interleukin-12- and gamma interferon-dependent protection against malaria conferred by CpG oligodeoxynucleotide in mice". Infect. Immun. 69(3):1643-1649 (2001).	
		GURA, "Antisense has growing pains". Science 270:575-576 (1995).	
		GURSEL, et al., "Differential and Competitive Activation of Human Immune Cells by Distinct Classes of CpG Oligodeoxynucleotide". J. Leuko. Biol. 71:813-820 (2002).	
		HADDEN, et al., "Immunopharmacology". JAMA 268(20):2964-2969 (1992).	
		HADDEN, et al., "Immunostimulants". TIPS 141:169-174 (1993).	
		HALPERN, et al., "Bacterial DNA induces murine interferon-gamma production by stimulation of interleukin-12 and tumor necrosis factor-alpha". Cell Immunol. 167(1):72-78 (1996).	
		HASLETT, et al., "Strong Human Immunodeficiency Virus (HIV) Specific CD4+ T Cell Responses in a Cohort of Chronically Infected Patients are Associated with Interruptions in Anti-HIV Chemotherapy". J. Infect. Diseases 181:1264-1272 (2000).	
		HATZFELD, "Release of early human hematopoietic progenitors from quiescence by antisense transformin owth factor β 1 or Rb oligonucleotides". J. Exp. Med. 174:925-929 (1991).	
		HAVLIR, et al., "Maintenance Antiretroviral Therapies in HIV-Infected Subjects with Undetectable Plasma HIV RNA after Triple-Drug Therapy". The New England Journal of Medicine 339(18):1261-1268 (1998).	
		HAYASHI, et al., "Enhancement of innate immunity against Mycobacterium avium infection by immunostimulatory DNA is mediated by indoleamine 2,3-dioxygenase". Infect. Immun. 69:6156-6164 (2001).	
		HERTL, et al., "Inhibition of Interferon- γ -Induced Intercellular Adhesion Molecule-1 Expression on Human Keratinocytes by Phosphorothioate Antisense Oligodeoxynucleotides is the Consequence of Antisense-Specific and Antisense-Non-Specific Effects". The Journal of Investigative Dermatology 104(5):813-818 (May 1995).	
		HIGHFIELD, "Sepsis: the more, the murkier". Biotechnology 12:828 (1994).	
		HOEFFLER, et al., "Identification of multiple nuclear factors that interact with cyclic adenosine 3',5'-monophosphate response element-binding protein and activating transcription factor-2 by protein-protein interactions". Mol. Endocrinol. 5(2):256-266 (1991).	

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		HONESS, et al., "Deviations from Expected Frequencies of CpG Dinucleotides in Herpesvirus DNAs May be Diagnostic of Differences in the States of Their Latent Genomes". J. Gen. Vir. 70(4):837-855 (1989).	
		HORSPOOL, et al., "Nucleic acid vaccine-induces immune responses require CD28 costimulation and are regulated by CTLA4". J. Immunol. 160:2706-2714 (1998).	
		HUGHES, et al., "Influence of Base Composition on Membrane Binding and Cellular Uptake of 10-mer Phosphorothioate Oligonucleotides in Chinese Hamster Ovary (CHRC5) Cells". Antisense Research and Development 4:211-215 (1994).	
		IGUCHI-ARIGA, et al., "CpG methylation of the cAMP-responsive enhancer/promoter sequence TGACGTCA abolishes specific factor binding as well as transcriptional activation". Genes Dev. 3(5):612-619 (1989).	
		IMAMI, et al., "Assessment of Type 1 and Type 2 Cytokines in HIV Type 1-Infected Individuals: Impact of Highly Active Antiretroviral Therapy". AIDS Research and Human Retroviruses 15(17):1499-1508 (1999).	
		ISHIBASHI, et al., "Sp1 Decoy Transfected to Carcinoma Cells Suppresses the Expression of Vascular Endothelial Growth Factor, Transforming Growth Factor β , and Tissue Factor and Also Cell Growth and Invasion Activities". Cancer Research 60:6531-6536 (2000).	
		ISHIKAWA, et al., "IFN induction and associated changes in splenic leukocyte distribution". J. Immunol. 150(9):3713-3727 (1993).	
		IVERSEN, et al., "Pharmacokinetics of an antisense phosphorothioate oligodeoxynucleotide against rev from human immunodeficiency virus type 1 in the adult male rat following single injections and continuous infusion". Antisense Res. Dev. 4:43-52 (1994).	
		JAKWAY, et al., "Growth regulation of the B lymphoma cell line WEHI-23 1 by anti-immunoglobulin, lipopolysaccharide, and other bacterial products". J. Immunol. 137(7):2225-2231 (1996).	
		JAROSZEWSKI, et al., "Cellular uptake of antisense oligonucleotides". Adv. Drug Delivery Rev. 6(3):235-250 (1991).	
		JILEK, et al., "Antigen-Independent Suppression of the Allergic Immune Response to Bee Venom Phospholipase A2 by DNA Vaccination in CBA/J Mice". J. Immunol. 166:3612-3621 (2001).	
		JONES, et al., "Synthetic Oligonucleotides Containing CpG Motifs Enhance Immunogenicity of a Peptide Malaria Vaccine in Aotus Monkeys". Vaccine 17:3065-3071 (1999).	
		JUFFERMANS, et al., "CpG oligodeoxynucleotides enhance host defense during murine tuberculosis". Infect. Immun. 70:147-152 (2002).	
		KADOWAKI, et al., "Distinct CpG DNA and Polyinosinic-Polycytidylic Acid Double Stranded RNA, Respectively, Stimulate CD11c- Type 2 Dendritic Cell Precursors and CD11c+ Dendritic cells to Produce Type I IFN". J. Immunol. 166:2291-2295 (2001).	
		KATAOKA, et al., "Antitumor activity of synthetic oligonucleotides with sequences from cDNA encoding proteins of Mycobacterium bovis BCG". Jpn. J. Cancer Res. 83:244-247 (1992).	

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		KHALED, et al., "Multiple mechanisms may contribute to the cellular anti-adhesive effects of phosphorothioate oligodeoxynucleotides". Nucleic Acids Research 24(4):737-745 (1996).	
		KIMURA, et al., "Binding of oligoguanylate to scavenger receptors is required for oligonucleotides to augment NK cell activity and induce IFN". J. Biochem 116(5):991-994 (1994).	
		KLINE, et al., "CpG motif oligonucleotides are effective in prevention of eosinophilic inflammation in a murine model of asthma". J. Invest. Med. 44(7):380A (1 page) (1996).	
		KLINE, et al., "CpG oligonucleotides can reverse as well as prevent TH2-mediated inflammation in a murine model of asthma". J. Invest. Med. 45(7):298A (1 page) (1997).	
		KLINE, et al., "Immune redirection by CpG oligonucleotides, Conversion of a Th2 response to a Th1 response in a murine model of asthma". J. Invest. Med. 45(3):282A (1 page) (1997).	
		KLINMAN, et al., "Immune recognition of foreign DNA: a cure for bioterrorism?". Immunity 11:123 (1 page) (1999).	
		KLINMAN, et al., "Repeated administration of synthetic oligodeoxynucleotides expressing CpG motifs provides long-term protection against bacterial infection". Infect. Immun. 67:5658-5663 (1999).	
		KLINMAN, et al., "CpG motifs present in bacteria DNA rapidly induce lymphocytes to secrete interleukin 6, interleukin 12, and interferon gamma". Proc. Natl. Acad. Sci. USA 93(7):2879-2883 (1996).	
		KLINMAN, et al., "Activation of the innate immune system by CpG oligodeoxynucleotides: immunoprotective activity and safety". Springer Semin. Immunopathol. 22:173-183 (2000).	
		KLINMAN, et al., "CpG Motifs as Immune Adjuvants". Vaccine 17:19-25 (1999).	
		KOU, et al., "Analysis and Regulation of interferon-gamma production by peripheral blood lymphocytes from patients with bronchial asthma". Arerugi 43(3):483-491 (1994), abstract only.	
		KRIEG, et al., "CpG motifs in bacterial DNA and their immune effect". Annu. Rev. Immunol. 20:709-760 (2002).	
		KRIEG, et al., "Brief Communication: Oligodeoxynucleotide Modifications Determine the Magnitude of B-Cell Stimulation by CpG Motifs". Antisense & Nucleic Acid Drug Development 6:133-139 (1996).	
		KRIEG, et al., "Phosphorothioate oligodeoxynucleotides: antisense or anti-protein?". Antisense Res. Dev. 5:241 (1 page) (1995).	
		KRIEG, et al., "Uptake of oligodeoxyribonucleotides by lymphoid cells is heterogeneous and inducible". Antisense Res. Dev. 1(2):161-171 (1991).	
		KRIEG, et al., "Leukocyte stimulation by oligodeoxynucleotides". Applied Antisense Oligonucleotide Tech. (BOOK):431-448 (1998).	
		KRIEG, et al., "Causing a Commotion in the Blood: Immunotherapy Progresses from Bacteria to Bacterial DNA". Immunology Today 21(10):521-526 (2000).	
		KRIEG, et al., "CpG DNA: A pathogenic factor in systemic lupus erythematosus?". J. Clin. Immunol. 15(6):284-292 (1995).	

EXAMINER
SIGNATURE:

DATE
CONSIDERED:

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		KRIEG, et al., "CpG DNA induces sustained IL-12 expression in vivo and resistance to Listeria monocytogenes challenge". J. Immunol. 161:2428-2434 (1998).	
		KRIEG, et al., "A role for endogenous retroviral sequences in the regulation of lymphocyte activation". J. Immunol. 143(8):2448-2451 (1989).	
		KRIEG, "An innate immune defense mechanism based on the recognition of CpG motifs in microbial DNA". J. Lab. Clin. Med. 128(2):128-133 (Abstract) (1996).	
		KRIEG, et al., "CpG motifs in bacterial DNA trigger direct B-cell activation". Nature 374:546-549 (1995).	
		KRIEG, et al., "Modification of antisense phosphodiester oligodeoxynucleotides by a 5' cholesteryl moiety increases cellular association and improves efficacy". Proc. Natl. Acad. Sci. USA 90:1048-1052 (1993).	
		KRIEG, et al., "The role of CpG dinucleotides in DNA vaccines". Trends in Microbiol. 6:23-27 (1998).	
		KRIEGER, et al., "Structures and Functions of Multiligand Lipoprotein Receptors: Macrophage Scavenger Receptors and LDL Receptor-Related Protein (LRP)". Annu. Rev. Biochem 63:601-637 (1994).	
		KRUG, et al., "Identification of CpG Oligonucleotide Sequences with High Induction of IFN- α/β in Plasmacytoid Dendritic Cells". Eur. J. Immunol. 31:2154-2163 (2001).	
		KRUG, et al., "Toll-like Receptor Expression Reveals CpG DNA as a Unique Microbial Stimulus for Plasmacytoid Dendritic Cells Which Synergizes With CD40 Ligand to Induce High Amounts of IL-12". Eur. J. Immunol. 31:3026-3037 (2001).	
		KUCHAN, et al., "Nucleotides in Infant Nutrition: Effects of Immune Function". Pediatr. Adolesc. Med. Basel. Karger 8:80-94 (1998).	
		KULKARNI, et al., "Effect of Dietary Nucleotides on Response to Bacterial Infection". J. Parenter. Enteral. Nutr. 10(2):169-171 Abstract (1986).	
		KURAMOTO, et al., "Oligonucleotide sequences required for natural killer cell activation". Jpn. J. Cancer Res. 83:1128-1131 (1992).	
		LAGRANGE, et al., "Immune Responses Directed Against Infectious and Parasitic Agents". Immunology (BOOK - ISBN:0471017604) (Chapter of Book; Ed - Jean-François Bach): (1978).	
		LANG, et al., "Guanosine-rich oligodeoxynucleotides induce proliferation of macrophage progenitors in cultures of murine bone marrow cells". Eur. J. Immunol. 29:3496-3506 (1999).	
		LAPATSCHEK, et al., "Activation of Macrophages and B Lymphocytes by an Oligodeoxynucleotide Derived from an Acutely Pathogenic Simian Immunodeficiency Virus". Antisense Nucleic Acid Drug Dev. 8(5):357-370 (Oct. 1998).	
		LEDERGERBER, et al., "Clinical Progression and Virological Failure on Highly Active Antiretroviral Therapy in HIV-1 Patients: a Prospective Cohort Study". The Lancet 353:863-868 (1999).	

EXAMINER SIGNATURE:	DATE CONSIDERED:
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		LEDERMAN, et al., "Polydeoxyguanine Motifs in a 12-mer Phosphorothioate Oligodeoxynucleotide Augment Binding to the v3 Loop of the HIV-1 gp120 and Potency of HIV-1 Inhibition Independently of G-Tetrad Formation". Antisense & Nucleic Acid Drug Development 6:281-289 (1996).	
		LEE, et al., "An Oligonucleotide Blocks Interferon- γ Signal Transduction". Transplantation 62(9):1297-1301 (1996).	
		LEIBSON, et al., "Role of γ -interferon in antibody-producing responses". Nature 309:799-801 (1984).	
		LEONARD, et al., "Conformation of guanine 8-oxoadenine base pairs in the crystal structure of d(CGCGAATT(O8A)GCG)". Biochemistry 31(36):8415-8420 (1992).	
		LI, et al., "Long-Lasting Recovery in CDR T-Cell Function and Viral -Load Reduction After Highly Active Antiretroviral Therapy in Advanced HIV-1 Disease". The Lancet 351:1682-1686 (1998).	
		LIANG, et al., "Activation of Human B Cells by Phosphorothioate Oligodeoxynucleotides". J. Clin. Invest. 98:1119-1129 (1996).	
		LIPFORD, et al., "CpG-containing synthetic oligonucleotides promote B and cytotoxic T cell responses to protein antigen: a new class of vaccine adjuvants". Eur. J. Immunol. 27(9):2340-2344 (1997).	
		LIPFORD, et al., "Immunostimulatory DNA: sequence-dependent production of potentially harmful or useful cytokines". Eur. J. Immunol. 27(12):3420-3426 (1997).	
		LÖNNBERG, et al., "Towards Genomic Drug Therapy with Antisense Oligonucleotides". Ann. Med. 28:511-522 (1996).	
		MACAYA, et al., "Thrombin-binding DNA aptamer forms a unimolecular quadruplex structure in solution". Proc. Natl. Acad. Sci. USA 90:3745-3749 (Apr.1993).	
		MACFARLANE, et al., "Antagonism of immunostimulatory CpG-oligodeoxynucleotides by quinacrine, chloroquine, and structurally related compounds". J. Immunol. 160(3):1122-1131 (1998).	
		MALTESE, et al., "Sequence context of antisense RelA/NF- κ B phosphorothioates determines specificity". Nucleic Acids Research 23(7):1146-1151 (1995).	
		MANZEL, et al., "Lack of Immune Stimulation by Immobilized CpG-oligonucleotide". Antisense & Nucleic Acid Drug Development 9(5):459-464 (1999).	
		MASTRANGELO, et al., "Gene therapy for human cancer: an essay for clinicians". Seminars Oncology 23(1):4-21 (1996).	
		MATSON, et al., "Nonspecific suppression of [3H]thymidine incorporation by control oligonucleotides". Antisense Res. Dev. 2(4):325-330 (1992).	
		MCCLUSKIE, et al., "Cutting Edge: CpG DNA Is a Potent Enhancer of Systemic and Mucosal Immune Responses Against Hepatitis B Surface Antigen with Intranasal Administration to Mice". J. Immun. 161:4463-4465 (1998).	

EXAMINER SIGNATURE:	DATE CONSIDERED:
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		MCCLUSKIE, et al., "Route and Method of DNA Vaccine Influence Immune Responses in Mice and Non-Human Primates". Molecular Med. 5(5):287-300 (1999).	
		MCINTYRE, et al., "A sense phosphorothioate oligonucleotide directed to the initiation codon of transcription factor NF-kappa B p65 causes sequence-specific immune stimulation". Antisense Res. Dev. 3(4):309-322 (1993).	
		MCKENZIE, "Nucleic Acid Vaccines". Immunologic Res. 24(3):225-244 (2001).	
		MERAD, et al., "In vivo Manipulation of Dendritic Cells to Induce Therapeutic Immunity". Blood 99(5):1676-1682 (2002).	
		MESSINA, et al., "Stimulation of in vitro murine lymphocyte proliferation by bacterial DNA". Cell Immunol. 147(6):1759-1764 (1991).	
		MESSINA, et al., "The influence of DNA structure on the in vitro stimulation of murine lymphocytes by natural and synthetic polynucleotide antigens". J. Immunol. 147:148-157 (1993).	
		MOJCIK, et al., "Administration of a phosphorothioate oligonucleotide antisense murine endogenous retroviral MCF env causes immune effect in vivo in a sequence-specific manner". Clin. Immunol. Immunopathol. 67(2):130-136 (1993).	
		MOTTRAM, et al., "A novel CDC2-related protein kinase from leishmania mexicana, LmmCRK1, is post-translationally regulated during the life cycle". J. Biol. Chem. 268(28):21044-21052 (1993).	
		NYCE, et al., "DNA antisense therapy for asthma in an animal model". Nature 385:721-725 (1997).	
		OBERBAUER, "Not nonsense but antisense - Applications of Antisense Oligonucleotides in Different Fields of Medicine". Wein Klin Wochenschr 109:40-46 (1997).	
		OGG, et al., "Quantitation of HIV-1-Specific Cytotoxic T-Lymphocytes and Plasma Load of Viral RNA". Science 279:2103-2106 (1998).	
		OKADA, et al., "Bone Marrow-Derived Dendritic Cells Pulsed With a Tumor-Specific Peptide Elicit Effective Anti-Tumor Immunity Against Intracranial Neoplasms". Int. J. Cancer 78:196-201 (1998).	
		PALUCKA, et al., "Dendritic Cells as the Terminal Stage of Monocyte Differentiation". J. Immunol. 160:4587-4595 (1999).	
		PAPASAVVAS, et al., "Enhancement of Human Immunodeficiency Virus Type I-Specific CD4 and CD8 T Cell Responses in Chronically Infected Persons after Temporary Treatment Interruption". J. Infect. Diseases 182:766-775 (2000).	
		PIALOUX, et al., "A Randomized Trial of Three Maintenance Regimens Given After Three Months of Induction Therapy with Zidovudine, Lamivudine, and Indinavir in Previously Untreated HIV-1-Infected Patients". The New England Journal of Medicine 339(18):1269-1276 (1998).	
		PISCITELLI, "Immune-Based Therapies for Treatment of HIV Infection". The Annals of Pharmacotherapy 30:62-76 (1996).	
		PISETSKY, et al., "Immunological Properties of Bacterial DNA". Ann. NY Acad. Sci. 772:152-163 (1995).	

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		PISETSKY, "Immunological consequences of nucleic acid therapy". Antisense Res. Dev. 5:219-225 (1995).	
		PISETSKY, "The immunological properties of DNA". J. Immunol. 156:421-423 (1996).	
		PISETSKY, et al., "Stimulation of murine lymphocyte proliferation by a phosphorothioate oligonucleotide with antisense activity for hepes simplex virus". Life Science 54:101-107 (1994).	
		PISETSKY, "Stimulation of in vitro proliferation of murine lymphocytes by synthetic oligodeoxynucleotides". Molecular Biol. Reports 18:217-221 (1993).	
		PLENAT, "Animal models of antisense oligonucleotides: lessons for use in humans". J. Mol. Med. Today 2(6):250-257 (1996).	
		PRASAD, et al., "Oligonucleotides Tethered to a Short Polyguanylic Acid Stretch are Targeted to Macrophages: Enhanced Antiviral Activity of a Vesicular Stomatitis Virus-Specific Antisense Oligonucleotide". Antimicrobial Agents and Chemotherapy 43(11):2689-2696 (Nov. 1999).	
		QUDDUS, et al., "Treating activated CD4+ T cells with either of two distinct DNA methyltransferase inhibitors, 5-azacytidine or procainamide, is sufficient to cause a lupus-like disease in syngeneic mice". J. Clin. Invest. 92(1):38-53 (1993).	
		RAMANATHAN, et al., "Characterization of the Oligodeoxynucleotide-mediated Inhibition of Interferon- γ -induced Major Histocompatibility Complex Class I and Intercellular Adhesion Molecule-1". The Journal of Biological Chemistry 269(40):24564-24574 (Oct.1994).	
		RAMANATHAN, et al., "Inhibition of Interferon- γ -Induced Major Histocompatibility Complex Class I Expression by Certain Oligodeoxynucleotides". Transplantation 57(4):612-615 (Feb. 1994).	
		RAZ, "Deviation of the Allergic IgE to an IgG Response by Gene Immunotherapy". Int. Rev. Immunol. 18(3):271-289 (1999).	
		RAZ, et al., "Preferential Induction of a Th1 Immune Response and Inhibition of Specific IgE Antibody Formation by Plasmid DNA Immunization". Proc. Natl. Acad. Sci. USA 93:5141-5145 (1996).	
		RAZ, et al., "Intradermal gene immunization: the possible role of DNA uptake in the induction of cellular immunity to viruses". Proc. Natl. Acad. Sci. USA 91:9519-9523 (1994).	
		RICCI, et al., "T cells, cytokines, IgE and allergic airways inflammation". J. Invest. Allergol Clin. Immunol. 4(5):214-220 (1994).	
		ROJANASAKUL, "Antisense oligonucleotide therapeutics: drug delivery and targeting". Drug Delivery Reviews 18:115-131 (1996).	
		ROMAN, et al., "Immunostimulatory DNA sequences function as T helper-1-promoting adjuvants". Nature Med. 3(8):849-854 (1997).	
		ROSENBERG, et al., "Immune Control of HIV-1 After Early Treatment of Acute Infection". Nature 407:523-526 (2000).	
		ROSENBERG, et al., "Vigorous HIV-1-Specific CD4+ T-Cell Responses Associated with Control of Viremia". Science 278:1447-1450 (1997).	

EXAMINER SIGNATURE:	DATE CONSIDERED:
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		RUIZ, et al., "Structured Treatment Interruption in Chronically HIV-1 Infected Patients After Long-Term Viral Suppression". AIDS 14:397-403 (2000).	
		SANTINI, et al., "Type I Interferon as a Powerful Adjuvant for Monocyte-derived Dendritic Cell Development and Activity In Vitro and in Hu-PBL-SCID Mice". J. Exp. Med. 191:1777-1788 (2000).	
		SATO, et al., "Immunostimulatory DNA sequences necessary for effective intradermal gene immunization". Science 273:352-354 (1996).	
		SCANLON, et al., "Oligonucleotide-mediated Modulation of Mammalian Gene Expression". FASEB J. 9:1288-1295 (1995).	
		SCHNELL, et al., "Identification and characterization of a Saccharomyces cerevisiae gene (PAR 1) conferring resistance to iron chelators". Eur. J. Biochem. 200:487-493 (1991).	
		SCHOOFS, "Small Steps -- A Limited Experiment Opens New Approach in Fight Against HIV". Wall Street Journal (Sep. 28, 2000).	
		SCHUBBERT, et al., "Ingested Foreign (phage M13) DNA Survives Transiently in the Gastrointestinal Tract and Enters the Bloodstream of Mice". Mol. Gen. Genet. 242:495-504 (1994).	
		SCHWARTZ, et al., "Endotoxin responsiveness and grain dust-induced inflammation in the lower respiratory tract". Am. J. Physiol. 267(5):609-617 (1994).	
		SCHWARTZ, et al., "The role of endotoxin in grain dust-induced lung disease". Am. J. Respir. Crit. Care Med. 152(2):603-608 (1995).	
		SCHWARTZ, et al., "CpG motifs in bacterial DNA cause inflammation in the lower respiratory tract". J. Clin. Invest. 100(1):68-73 (1997).	
		SEDEGAH, et al., "Intertukin 12 induction of interferon g-dependent protection against malaria". Proc. Natl. Acad. Sci. USA 91:10700-10792 (1994).	
		SETHI, et al., "Postexposure prophylaxis against prion disease with a stimulator of innate immunity". Lancet 360:229-230 (2002).	
		SHAFFER, et al., "Highly Active Antiretroviral Therapy (HAART) for the Treatment of Infection With Human Immunodeficiency Virus Type 1". Biomed. & Pharmacother. 53:73-86 (1999).	
		SHIRAKAWA, et al., "The inverse association between tuberculin responses and atopic disorder". Science 275(5296):77-79 (1997).	
		SIDMAN, et al., "γ-Interferon is one of several direct B cell-maturing lymphokines". Nature 309:801-804 (1984).	
		SPARWASSER, et al., "Macrophages sense pathogens via DNA motifs: induction of tumor necrosis factor-α-mediated shock". Eur. J. Immunol. 27(7):1671-1679 (1997).	
		SPARWASSER, et al., "Bacterial DNA and immunostimulatory CpG oligonucleotides trigger maturation and activation of murine dendritic cells". Eur. J. Immunol. 28:2045-2054 (1998).	
		SPIEGELBERG, et al., "Recognition of T Cell Epitopes and Lymphokine Secretion by Rye Grass Allergen Lolium perenne I-Specific Human T Cell Clones". J. of Immunology 152:4706-4711 (1994).	

EXAMINER
SIGNATURE:

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		STACEY, et al., "Immunostimulatory DNA as an adjuvant in vaccination against Leishmania major". Infect. Immun. 67:3719-3726 (1999).	
		STEIN, et al., "Oligodeoxynucleotides as inhibitors of gene expression: a review". Cancer Res. 48:2659-2668 (1998).	
		STULL, et al., "Antigene, ribozyme, and aptamer nucleic acid drugs: progress and prospects". Pharm. Res. 12(4):465-483 (1995).	
		SU, et al., "Vaccination against Chlamydial Genital Tract Infection after Immunization with Dendritic Cells Pulsed Ex Vivo with Nonviable Chlamydiae". J. Exp. Med. 188:809-818 (1998).	
		SUBRAMANIAN, et al., "Theoretical considerations on the 'spine of hydration' in the minor groove of d(CGCGAATTCGCG) d(CGGCTTAAGCGC): Monte Carlo computer simulation". Proc. Natl. Acad. Sci. USA 85:1836-1840 (1988).	
		SYME, et al., "Generation of Dendritic Cells ex vivo: Differences in Steady State versus Mobilized Blood from Patients with Breast Cancer, with Lymphoma, and from Normal Donors". J. Hematother. Stem Cell Res. 10:621-630 (2001).	
		TANAKA, et al., "An antisense oligonucleotide complementary to a sequence in I gamma 2b increases gamma 2b germine transcripts, stimulates B cell DNA synthesis and inhibits immunoglobulin secretion". J. Exp. Med. 175:597-607 (1992).	
		TARTE, et al., "Extensive characterization of dendritic cells generated in serum-free conditions: regulation of soluble antigen uptake, apoptotic tumor cell phagocytosis, chemotaxis and T cell activation during maturation in vitro". Leukemia 14:2182-2192 (2000).	
		THORNE, "Experimental grain dust atmospheres generated by wet and dry aerosolization techniques". Am. J. Ind. Med. 25(1):109-112 (1994).	
		TIGHE, et al., "Conjunction of Protein to Immunostimulatory DNA results in a Rapid Long-Lasting and Potent Induction of Cell-Mediated and Humoral Immunity". Eur. J. Immunol. 30:1939-1947 (2000).	
		TOKUNAGA, et al., "A synthetic single-stranded DNA, poly(dG, dC), induces interferon- α/β and - γ , augments natural killer activity and suppresses tumor growth". Jpn. J. Cancer Res. 79:682-686 (1988).	
		TOKUNAGA, et al., "Synthetic oligonucleotides with particular base sequences from the cDNA encoding proteins of Mycobacterium bovis BCG induce interferons and activate natural killer cells". Microbiol. Immunol. 36(1):55-66 (1992).	
		UHLMANN, et al., "Antisense oligonucleotides: a new therapeutic principle". Chem. Rev. 90:543-584 (1990).	
		VERDIJK, et al., "Polyriboinosinic Polyribocytidylic Acid (Poly(I:C)) Induces Stable Maturation of Functionally Active Human Dendritic Cells". J. Immunol. 163:57-61 (1999).	
		VERMA, et al., "Gene therapy - promises, problems and prospects". Nature 389:239-242 (Sep.1997).	

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		VIL'NER, "Effect of Amphotericin B on the interferonogenic activity of poly(G).poly (C) and poly(G,I).poly(C) in mice and their resistance to infection by the tick-borne encephalitis virus". Antibiotiki 27(11):827-830 (Nov. 1982), abstract only.	
		VIL'NER, et al., "Effect of virazole on the antiviral activity of poly(G) X poly© and other polyribonucleotide interferogens". Antibiotiki 29(6):450-453 (1984), abstract only.	
		VIL'NER, et al., "Evaluation of the size of the continuous poly(G) site necessary for the biological activity of the poly(G).poly(C) complex". Vopr Virusol 30(3):337-340 (1985), abstract only.	
		VIL'NER, "Effect of the size of the continuous poly(G) site in poly(G,A).poly(C) complexes on their interferon-inducing activity and their capacity to stimulate the development of the immunity". Vopr Virusol 31(6):697-700 (1986), abstract only.	
		VIL'NER, et al., "Dependence of the antiviral activity of the poly(G).poly(C) complex on the size of the continuous poly(C) segments". Vopr Virusol 33(3):331-335 (1988), abstract only.	
		WAGNER, "Bacterial CpG DNA Activates Immune Cells to Signal Infectious Danger". Adv. Immunol. 73:329-368 (1999).	
		WAGNER, "Gene inhibition using antisense oligodeoxynucleotides". Nature 372:333-335 (1994).	
		WALKER, et al., "Activated T Cells and Cytokines in Bronchoalveolar Lavages from Patients with Various Lung Diseases Associated with Eosinophilia". Am. J. Respir. Crit. Care Med. 150:1038-1048 (1994).	
		WALKER, et al., "Immunostimulatory oligodeoxynucleotides promote protective immunity and provide systemic therapy for leishmaniasis via IL-12- and IFN-g-dependent mechanisms". Proc. Natl. Acad. Sci. USA 96:6970-6975 (1999).	
		WALLACE, et al., "Oligonucleotide probes for the screening of recombinant DNA libraries". Methods Enzymol. 152:432-442 (1987).	
		WEINER, "The immunobiology and clinical potential of immunostimulatory CpG oligodeoxynucleotides". Leukocyte Bio. 68:455-463 (2000).	
		WEINER, et al., "Immunostimulatory oligodeoxynucleotides containing the CpG motif are effective as immune adjuvants in tumor antigen immunization". Proc. Natl. Acad. Sci. USA 94:10833-10837 (1997).	
		WEISS, "Upping the antisense ante: scientists bet on profits from reverse genetics". Science 139:108-109 (1991).	
		WHALEN, et al., "DNA-Mediated Immunization to the Helatitis B Surface Antigen: Activation and Entrainment of the Immune Response". Ann. NY Acad. Sci. 772:64-76 (1995).	
		WHALEN, "DNA vaccines for emerging infection diseases: what if?". Emerg. Infect. Dis. 2(3):168-175 (1996).	
		WLOCH, et al., "The influence of DNA sequence on the immunostimulatory properties of plasmid DNA vectors". Hum. Gene Ther. 9(10):1439-1447 (Jul. 1998).	
		WOOLRIDGE, et al., "Immunostimulatory oligodeoxynucleotides containing CpG motifs enhance the efficacy of monoclonal antibody therapy of lymphoma". Blood 89:2994-2998 (1997).	

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<p align="center">SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p>		Attorney Docket Number	4239-66899-01
		Application Number	10/666,022
		Filing Date	September 17, 2003
		First Named Inventor	Klinman
		Art Unit	1645
		Examiner Name	Nita Minnifield
Examiner's Initials*	Cite No. (optional)	OTHER DOCUMENTS	
		WU, et al., "Receptor-mediated gene delivery and expression in vivo". J. Biol. Chem. 263:14621-14624 (1988).	
		WU-PONG, "Oligonucleotides: opportunities for drug therapy and research". Pharmaceutical Tech. 18:102-114 (1994).	
		WYATT, et al., "Combinatorially selected guanosine-quartet structure is a potent inhibitor of human immunodeficiency virus envelope-mediated cell fusion". Proc. Natl. Acad. Sci. USA 91:1356-1360 (Feb. 1994).	
		YAMAMOTO, et al., "Ability of oligonucleotides with certain palindromes to induce interferon production and augment natural killer cell activity is associated with their base length". Antisense Res. Dev. 4:119-123 (1994).	
		YAMAMOTO, "Unique palindromic sequences in synthetic oligonucleotides are required to induce inf and augment INF-mediated natural killer activity". J. Immunol. 148(12):4072-4076 (1992).	
		YAMAMOTO, et al., "In vitro augmentation of natural killer cell activity and production of interferon-alpha/beta and -gamma with deoxyribonucleic acid fraction from Mycobacterium bovis BCG". Jpn. J. Cancer Res. 79:866-873 (1988).	
		YAMAMOTO, et al., "Synthetic oligonucleotides with certain palindromes stimulate interferon production of human peripheral blood lymphocytes in vitro". Jpn. J. Cancer Res. 85:775-779 (1994).	
		YAMAMOTO, et al., "Mode of action of oligonucleotide fraction extracted from Mycobacterium bovis BeG". Kekkaku 69(9):29-32 (1994).	
		YAMAMOTO, et al., "DNA from bacteria, but not vetebrates, induces interferons, activates natural killer cells, and inhibits tumor growth". Microbiol. Immunol. 36(9):983-997 (1992).	
		YAMAMOTO, et al., "Lipofection of synthetic oligodeoxyribonucleotide having a palindromic sequence AACGTT to murine splenocytes enhances interferon production and natural killer activity". Microbiol. Immunol. 38(10):831-836 (1994).	
		YASWEN, et al., "Effects of Sequence of Thioated Oligonucleotides on Cultured Human Mammary Epithelial Cells". Antisense Research and Development 3:67-77 (1993).	
		YEW, et al., "Contribution of Plasmid DNA to Inflammation in the Lung After Administration of Cationic Lipid: pDNA Complexes". Hum. Gene Ther. 10(2):223-234 (1999).	
		YI, et al., "IFN-γ promotes IL-6 and 1gM secretion in response to CpG motifs in bacterial DNA and oligonucleotides". J. Immunol. 156:558-564 (1996).	
		YI, et al., "Rapid immune activation by CpG motifs in bacterial DNA". J. Immunol. 157:5394-5402 (1996).	
		ZELPHATI, et al., "Inhibition of HIV-1 Replication in Cultured Cells with Antisense Oligonucleotides Encapsulated in Immunoliposomes". Antisense Res. Dev. 3:323 (1993).	
		ZHANG, et al., "Antigen- and Isotype-Specific Immune Responses to a Recombinant Antigen-Allergen Chimeric (RAAC) Protein". J. Immunol. 151:791-799 (1993).	

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		ZHAO, et al., "Comparison of cellular binding and uptake of antisense phosphodiester, phosphorothioate, and mixed phosphorothioate and methylphosphonate oligonucleotides". Antisense Res. Dev. 3(1):53-66 (1993).	
		ZHAO, et al., "Stage-specific oligonucleotide uptake in murine bone marrow B-cell precursors". Blood 84(11):3660-3666 (1994).	
		ZHENG, et al., "Contribution of Vascular Endothelial Growth Factor in the Neovascularization Process During the Pathogenesis of Herpetic Stromal Keratitis". J. Virol. 75(20):9828-9835 (2001).	
		ZHU, et al., "Macaque blood-derived antigen-presenting cells elicit SIV-specific immune responses". J. Med. Primatol 29:182-192 (2000).	
		ZIMMERMANN, et al., "CpG oligodeoxynucleotides trigger protective and curative Th1 responses in lethal murine leishmaniasis". J. Immunol. 160:3627-3630 (1998).	

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